Interim Guidelines for Smallpox Response and Management in the Post-Eradication era

These are interim guidelines and will need to be modified as the structure and functions of the Health Protection Agency evolve.

The Department of Health Communicable Diseases branch wishes to thank the Chair and members of the expert subgroup of the Joint Committee of Vaccination and Immunisation and all the clinical, microbiological and public health practitioners across the U.K., who have contributed to the development of this plan.
2nd December 2002

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Important: please include your name and profession in your e-mail.
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I  Background

1. Following global eradication of smallpox in 1980, the smallpox virus has been retained legally under strict security in two World Health Organisation (WHO) collaborating centres: the Centre for Disease Control and Prevention (CDC), Atlanta, USA and the Laboratory for Applied Microbiology at Koltsovo in Novosibirsk Region, Russian Federation.

2. Although it is highly unlikely, concern remains that illicitly obtained smallpox virus could be deliberately released as a biological weapon. Without containment measures, this would almost certainly lead to rapid spread because:
   - The majority of the population of the United Kingdom - as elsewhere - is susceptible, vaccination having ceased in the 1970s.
   - Population mobility is far greater than thirty years ago.
   - There may be delays in diagnosing the disease due to clinicians’ unfamiliarity with the presenting features.

3. Since the public health consequences would be severe, it is essential that contingency plans are available nationally and locally should smallpox re-emerge in the UK or elsewhere in the world.

4. This interim plan outlines the strategies and approaches that would guide national and local responses to a smallpox emergency. It is based on the “Memorandum on the Control of Outbreaks of Smallpox” published in 1975 by the Department of Health and Social Security and the Welsh Office.
II Introduction

5. Smallpox (variola) was one of the most severe infectious diseases affecting humans. It was present throughout the world during most of recorded history. It is specifically a human disease with no reservoir in any animal species. The infection no longer exists in nature, having been declared eradicated in 1980 following a global campaign led by the WHO.

6. Smallpox virus is a DNA virus. It is a member of the genus orthopox virus, which includes vaccinia and monkeypox. Only smallpox is readily transmissible from person to person.

7. The last community-acquired case was in Somalia in 1977. Following eradication in 1980 the WHO recommended that all countries cease vaccination. Routine vaccination in the UK and other European countries had ceased prior to this in the 1970s. Knowledge of the natural history of smallpox is from historical records and the personal experience of a relatively small number of senior physicians, microbiologists and epidemiologists who dealt with the disease in the past.

8. Patients are infectious with the onset of fever (see Section IV), however the typical vesicular rash (see Section III) does not appear until 4 to 7 days later. The rash is preceded by a prodromal period of 1 to 3 days of fever, malaise, headache and backache followed by 2 to 4 days of a macular rash. Clinical pictures to illustrate the rash can be found on the PHLS website: http://www.phls.org.uk/topics_az/smallpox/pictures.htm

9. Control and ultimately eradication of smallpox was achieved by vaccination. The vaccine is based on vaccinia virus, a live virus of low pathogenicity. Although effective in the eradication of smallpox, the vaccine can cause serious adverse effects, and for this reason vaccination in the UK was discontinued in the 1970s because the risks from vaccination outweighed the risks from disease. In the absence of any clear evidence that smallpox may re-emerge, this remains the case. In the event of an outbreak, the containment strategy will centre on isolation of cases and vaccination of contacts. However, it is planned that sufficient supplies will be available to vaccinate the entire population of the UK should this be deemed necessary.

10. The duration of complete immunity provided by vaccination is uncertain, but is unlikely to be more than 10 years. Previously vaccinated individuals are therefore unlikely to be protected from infection although the disease may be less severe. They will develop immunity more quickly on revaccination.
III Natural history and typical features of variola major in a non-immune individual

Clinical features

11. Smallpox has two distinct clinical forms: variola major, which produces severe smallpox, and variola minor, which is a much milder disease. Approximately 90% of cases of variola major in non-immune individuals would be expected to have the characteristic clinical presentation described in paragraph 13.

12. Following infection, asymptomatic viraemia develops on the third or fourth day, followed by dissemination and replication in the spleen, bone marrow and lymphoid tissues. A secondary viraemia begins around the eighth day and is associated with onset of a characteristic illness around 12 days following exposure (see incubation period in Section IV).

13. Variola major has a characteristic clinical presentation The illness progresses as outlined below (see also the clinical pictures on the PHLS website: http://www.phls.org.uk/topics_az/smallpox/pictures.htm

- Sudden onset of high fever with malaise, prostration, headache and backache.
- A macular rash develops 1 to 3 days later, firstly on the oral and pharyngeal mucosa, spreading to the face and forearms, trunk and legs.
- The macular rash becomes papular after 1 to 2 days and then vesicular after a further 1 to 2 days. The vesicular rash is typically more prominent on the face and extremities than on the trunk (centrifugal distribution).
- The vesicular rash becomes pustular after a further 2 to 3 days. Pustules are round, tense and deep in the dermis. They may affect the palms of the hands and soles of the feet.
- Vesicles and pustules are typically at the same stage of development in any area of skin.
- The pustules form scabs after 5 to 8 days.
- The scabs gradually separate leaving characteristic pitted scarring. The scars are most evident on the face.

Laboratory features

14. Full blood count shows a lymphocytosis or a predominance of lymphocytes, with many atypical and activated mononuclear cells. Haemorrhagic disease is preceded by a fall in the platelet count.
Differential diagnosis

15. Experience from the global eradication campaign was that atypical cases of chickenpox (varicella-zoster virus (VZV)) and disseminated herpes simplex virus (HSV) infection presented the greatest difficulties in the differential diagnosis.

16. Chickenpox can be distinguished from smallpox by its much more superficial lesions, their presence on the trunk rather than on the face and extremities (centripetal distribution), and by the development of successive crops of lesions in the same area (ie. lesions at different stages of development). The WHO has produced training materials to help health staff recognise smallpox, distinguish it from chickenpox, and avoid diagnostic errors. These materials are available electronically: http://www.who.int/emc/diseases/smallpox/smallpox-english.ppt

17. Disseminated HSV infection may also present a problem for differential diagnosis. However, VZV and HSV are both herpes viruses, and should be readily distinguished from orthopox virus particles by EM of vesicular fluid preparations.

18. Other causes of rash such as measles, enterovirus, parvovirus B19 or rubella may also cause uncertainty but should be distinguishable clinically, as well as in the laboratory. Molluscum contagiosum is also an orthopox virus, but is usually distinguishable from smallpox on clinical grounds (lesions are umbilicated from an early stage and the patient is well) and in the laboratory.

19. The final diagnosis in consultations for suspected smallpox with a single UK smallpox panellist are listed in table 1. These were made over a 20 year period in an immunised population, during which there was one outbreak of variola major and one of variola minor

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>4</td>
</tr>
<tr>
<td>No diagnosis, but proved not smallpox (3 cases required isolation)</td>
<td>15</td>
</tr>
<tr>
<td>Chickenpox</td>
<td>113</td>
</tr>
<tr>
<td>Papular vesicular urticaria</td>
<td>34</td>
</tr>
<tr>
<td>Generalised vaccinia and other reactions to vaccination</td>
<td>23</td>
</tr>
<tr>
<td>Staphylococcal folliculitis</td>
<td>9</td>
</tr>
<tr>
<td>Erythema multiforme</td>
<td>9</td>
</tr>
<tr>
<td>Scabies</td>
<td>6</td>
</tr>
<tr>
<td>Bacterial septicaemias</td>
<td>4</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>3</td>
</tr>
<tr>
<td>Secondary syphilis</td>
<td>2</td>
</tr>
<tr>
<td>Others included measles, coxsackie, acute leukaemia, anaphylactoid purpura, fungal infections, septic spots, insect bites, pityriasis rosea, sweat rash</td>
<td>18</td>
</tr>
</tbody>
</table>
Mortality

20. Estimates of mortality are complicated by the fact that documented epidemics were modified by the presence of some immune individuals in the population or by interventional vaccination. Importation into smallpox naïve and unvaccinated populations caused the highest mortality.

21. Some clinical forms of smallpox were highly virulent (variola major) and others much less so (variola minor). The highest mortality was seen in children aged less than 1 year, in the elderly, in pregnant women who were more susceptible to haemorrhagic disease, and in people immunocompromised due to medical disorders or treatments. There are now many more vulnerable individuals in the elderly and immunocompromised groups than in the past.

Atypical presentations

22. Along with the typical presentation of smallpox, two other rare forms are described: haemorrhagic and malignant smallpox.

23. Cases of haemorrhagic smallpox were uniformly fatal. They occurred among all ages and in both sexes, with pregnant women particularly susceptible. Haemorrhage into the mucous membranes and the skin accompanied the rash. Haemorrhagic smallpox was most commonly misdiagnosed as haemorrhagic chickenpox, meningococcal septicaemia or acute leukaemia.

24. Cases of malignant smallpox were characterised by lesions that did not develop to the pustular stage but remained soft and flat.

Modified smallpox

25. Vaccinated individuals may develop a mild disease, with similar prodromal features, but only a few atypical lesions, and a mortality of well under 1%. Note however that they are still infectious.
IV Epidemiology

Incubation period

26. For smallpox, this is usually defined as the time between exposure and onset of fever. The range given by most authorities is 7 to 17 days, usually 10 to 16 days, with a median of 12 days. The typical vesicular rash appears 4 to 7 days later.

Transmission

27. There is no known animal reservoir or vector for the smallpox virus. The most frequent mode of transmission is person-to-person spread via direct inoculation of infective droplets onto the oral, nasopharyngeal or respiratory mucosa during close contact with an infectious individual. From the mucosa the virus is transferred to local lymphoid tissue where replication occurs.

28. Patients are not infectious during the asymptomatic incubation period. They become infectious with the onset of fever. Infectiousness then increases until the onset of vesicular rash and remains high for the next 7 days. As a precaution, for the purpose of contact tracing, patients should be regarded as infectious from 24 hours prior to the time when fever was first recognised.

29. Patients remain infectious until the last scabs fall off. As a precaution, WHO isolation policy during the eradication campaign required that patients remain in isolation, in hospital or at home, until the last scab had separated. However, the virus shed from the skin is not highly infectious and exposure to patients in the late stages of the disease is unlikely to produce infection in susceptible contacts.

30. The most efficient transmission of smallpox occurred during close contact with infected persons. Household contact produces the highest attack rate, and contact in an open ward was a major cause of spread. In outbreaks in Asia and Africa, the attack rate in households varied from 37% to 96%, with some of the variation probably related to different living conditions and crowding, as well as to strain variation among variola viruses.

31. Casual contact, such as working in the same building, is much less likely to result in infection, although airborne spread of virus in draughts or air conditioning systems is known to cause transmission. Contaminated clothing or bed linen can also spread the virus.
**Organism survival**

32. In normal environmental conditions (ambient temperature, ordinary levels of humidity and exposure to sunlight) the virus is very unlikely to survive for more than 48 hours.

33. Depending on the conditions, variola viruses can survive for long periods in dry scabs (13 years has been documented), however this is not considered to represent an infectious threat.
V Case definitions and laboratory investigation

34. The preliminary definitions given below may require revision by clinicians and public health personnel depending upon the scale of the outbreak.

35. **Clinical case definition.** An illness with acute onset of fever >38°C, which is persistent, followed by a rash without other apparent cause characterised by vesicles or firm pustules at the same stage of development and with a predominantly centrifugal distribution.

36. The case definition in paragraph 35 describes the typical presentation of smallpox. The predictive value of this clinical case definition is likely to be low in the absence of circulating smallpox. Atypical presentations (haemorrhagic and malignant), and modified smallpox must also be considered.

37. **Laboratory criteria for confirmation.** Smallpox viruses are classified as Hazard Group 4 organisms and must be handled accordingly. Clinical samples from suspected cases must be handled with due regard to the likelihood that smallpox is present, and the appropriate procedures observed. Should it be necessary to conduct work other than in a Category 4 laboratory, a full risk assessment must be conducted.

38. The importance, and methods, of laboratory confirmation depend on the epidemiological situation:
   - **Electron microscopy (EM).** In the initial cases or unrelated cases in a new geographical area, EM identification of orthopox virus in a patient with symptoms compatible with the clinical case definition indicates a probable case of smallpox – see paragraph 43. During an outbreak, in the presence of an epidemiological link to other confirmed cases, EM identification of orthopox virus may be regarded as confirmatory.
   - **Polymerase chain reaction (PCR) and viral isolation from culture (Category 4 laboratories only).** Confirmation using these techniques is required for initial cases or unrelated cases in a new geographical area. They may also be of critical importance in distinguishing cases of variola and generalised vaccinia. Definitive diagnosis of smallpox will be based on the DNA sequence of PCR amplicons and the characteristics of viral isolates.

39. EM takes 2 hours and PCR takes 6 hours from receipt of specimens until results can be provided.
40. In a case with strongly suspicious clinical features and no other diagnosis, failure to detect any organism with EM or PCR does not exclude smallpox, and such cases may be regarded as probable.

41. If a large outbreak occurs, laboratory capacity will soon be overwhelmed. In this instance, priority for laboratory resources will include:
   • Testing of clinical specimens from cases with unclear clinical presentations following expert assessment.
   • Testing of clinical or environmental specimens that will provide information about a potential source of exposure to facilitate case detection and law enforcement activities.

In these circumstances, specimens will be triaged by local Infectious Disease Physicians, Virologists and Public Health Physicians, according to guidelines issued by the National and Regional Smallpox Outbreak Control Centres.

Case Classification

42. **Suspected**: a case of fever and rash consistent with the case definition (see paragraph 35), without laboratory confirmation or an epidemiological link to other cases. Initial cases of smallpox, or unrelated cases in a new geographical area are likely to present as suspected cases.

43. **Probable**: a case of fever and rash consistent with the case definition, plus:
   • For initial cases of smallpox or unrelated cases in a new geographical area - EM identification of orthopox virus or a case with strongly suspicious clinical features and no other diagnosis.
   • During an outbreak - an epidemiological link to a confirmed case.

44. **Confirmed**: a case of fever and rash consistent with the case definition, plus:
   • For initial cases of smallpox or unrelated cases in a new geographical area - laboratory confirmation by PCR or viral isolation.
   • During an outbreak - an epidemiological link to a confirmed case and EM identification of orthopox virus or a case with strongly suspicious clinical features and no other diagnosis.

45. **Possible**: acute onset of fever but no rash in a person with an epidemiological link to a confirmed case. The fever may be accompanied by prodromal symptoms such as prostration, severe headache or backache, rigors and generalised maculopapular rash. Control of an outbreak will depend on early identification and management of possible cases.
Table 2: summary of minimum criteria for case classification

<table>
<thead>
<tr>
<th>Classification</th>
<th>Fever</th>
<th>Rash</th>
<th>EM identification of orthopox</th>
<th>PCR positive for smallpox</th>
<th>Epidemiological link to another confirmed case of smallpox</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected (Initial cases or during outbreak)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Probable: Initial cases</td>
<td>+</td>
<td>+</td>
<td>+/±</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>During outbreak</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Confirmed: Initial cases</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>During outbreak</td>
<td>+</td>
<td>+</td>
<td>+/±</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Possible (During outbreak)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

* Fever and rash consistent with the case definition – see paragraph 35.
# EM not required if the case has strongly suspicious clinical features with no other diagnosis.

46. The diagnosis of suspected or probable cases according to the clinical case definition requires assessment by a Smallpox Diagnostic Expert – see Sections VI.

Laboratory networks

47. The collection and transport of clinical specimens from suspected smallpox cases, including the equipment and procedures for taking specimens is described in Appendix 1.

48. Laboratory testing of clinical specimens from initial suspected cases will involve EM at one of the designated Category 3 Regional laboratories (see Appendix 2), followed by confirmation by PCR at a Reference Laboratory.

49. Rapid real-time PCR tests for orthopox, varicella zoster and herpes simplex viruses are currently being evaluated, and it is planned that these could be made available to selected Category 3 Regional laboratories in the future.

50. Pre-exposure vaccination is required for staff who might be involved in handling clinical specimens from the initial suspected cases. At Alert Level 0 (see Section VI and Appendix 3), a small number of staff at designated Category 3 Regional laboratories and the Reference laboratories will be vaccinated (see Section VIII). In the event of an Alert Level 1, a larger number of laboratory staff will be vaccinated in case they are required to handle specimens.
51. It is possible that viral particles resembling smallpox may be identified on routine EM of vesicular fluid. In this event, the specimen should be sent immediately to a Reference laboratory according to the procedures described in Appendix 1. The virologist must also immediately inform the referring clinician who should arrange for a Smallpox Diagnostic Expert to assess the patient – see Section VI.
VI  Planning for outbreaks of smallpox

52. Since smallpox no longer exists as a naturally acquired infection, the two most likely causes for its re-emergence would be:
   • A deliberate release of the organism. This may occur without warning and it is possible that many people would be exposed, either via infected person(s) or environmental release of smallpox virus. A criminal investigation would need to proceed in parallel with the public health response.
   • An accidental release in one of the two approved collaborating centres for smallpox. This is unlikely because both laboratories undergo frequent WHO inspections and have stringent safety and security procedures in place.

53. A number of Alert Levels can be identified to assist planning according to the actions required (see Appendix 3). Alert Levels proceed in a stepwise fashion, except that level 0 may proceed directly to levels 1 or 2.
   • Alert Level 0: Smallpox remains eradicated - no credible threat of a release.
   • Alert Level 1: Heightened threat:
     q Case confirmed outside UK.
     q Virus identified outside the WHO approved collaborating centres.
     q Intelligence suggests a credible and imminent threat of a release in the UK.
   • Alert Level 2: Case confirmed in the UK.
   • Alert Level 3: Outbreak occurring in the UK.
   • Alert Level 4: Large or multiple outbreak not controlled by ring vaccination.
   • Alert Level 5: Outbreak controlled – no further cases occurring.

Diagnosis and response to initial cases

54. Early recognition and appropriate management of initial cases is key to rapid implementation of outbreak containment measures. At Alert Levels 0 and 1, the aim will be to alert clinicians to the possibility of a case of smallpox, raise awareness of the presenting symptoms and signs, and encourage appropriate and rapid reporting of patients with suspicious illnesses for further assessment. Structures and processes for further assessment and management of these patients will also be required.
Regional Smallpox Diagnosis and Response Groups and Teams (RSDRG and RSDRT)

55. **Regional Smallpox Diagnosis and Response Groups** will be established in each Standard Government Region at Alert Level 0. Each Unit will be headed by the Regional Epidemiologist (RE) on behalf of the Regional Director of Public Health (RDPH), and will be accountable dually through the Health Protection Agency (HPA) and the Department of Health (DH).

56. RSDRGs will be responsible for all aspects of planning for outbreaks of smallpox:
- Maintain a **24 hour emergency response** to suspected and probable cases of smallpox through RSDRTs (see below).
- **Co-ordinate vaccinations** to be provided at Alert Levels 0 and 1 (see Section VIII) and monitor vaccine side effects.
- **Identify healthcare, emergency, laboratory and other essential personnel** who will be vaccinated at Alert Levels 1 and 2.
- Identify a Regional **Smallpox Care Centre** (see Appendix 6).
- Identify a Regional **Smallpox Vaccination Centre** (see Appendix 8).
- Train and co-ordinate a **network of Smallpox Diagnostic Experts** (see below)
- Offer a **resource for training clinicians** in the recognition and reporting of patients with suspicious illnesses.
- Distribute a National Standard **Diagnostic Algorithm** to clinicians through PCTs to aid the assessment of patients with suspicious illnesses – see Figure 10.
- Develop **multi-agency partnerships** with the designated Regional Category 3 laboratory and with local emergency services across the Region to ensure that a co-ordinated response can be mounted to the first suspected or probable cases.

57. At Alert Level 0, each RSDRG will have five **Regional Smallpox Diagnosis and Response Teams**. One of these Teams will be on duty at all times to respond to suspected and probable cases of smallpox. They will be contactable through a single emergency telephone number maintained by the RSDRG.

58. Each RSDRT will comprise five members: a **Public Health Physician** (who is team leader), a **Medical Consultant** (usually an ID Physician), a **Communicable Disease Control Nurse**, a **Clinical Nurse** with experience in acute emergency medicine, and a **Paediatrician**. One individual in each role will be on duty at all times. All members of the team will be vaccinated against smallpox (see Section VIII). The equipment to be carried by Teams is listed in Appendix 4. They will be given training in smallpox management and additional general emergency medical training such as Advanced Life Support.
59. At Alert Level 1, the number of RSDRTs per RSDRG will be increased to allow a response to multiple cases arising simultaneously.

**Smallpox Diagnostic Experts (SDE)**

60. **Smallpox Diagnostic Experts** will be Infectious Disease (ID) Physicians who, at Alert Level 0, will be vaccinated against smallpox (see Section VIII) and given advanced training in smallpox differential diagnosis so that they are able to assess patients with suspicious illnesses safely and accurately.

61. ID Physicians in each Region will be invited by the RSDRG to become SDEs, and a network of SDEs will be established who will be trained and co-ordinated by the RSDRG.

62. At Alert Levels 1 or 2, more ID physicians and possibly consultants from other specialties will be trained as SDEs.

**Procedure for assessment and management of initial cases**

63. Patients with suspicious illnesses may present at a variety of different sites as listed below (in addition, smallpox virus may be seen on routine EM of vesicular fluid – see paragraph 51). General and specific management in the event of each of these scenarios is described in Figures 1 to 7.

- At a patient’s home.
- At a primary care centre.
- At a hospital:
  - Accident and Emergency (A+E),
  - General Medical ward,
  - Intensive Care Unit (ICU), or
  - Infectious Disease (ID) Unit.
- At a Port Health Control Unit.

64. Clinicians will be offered training and a National Standard **Diagnostic Algorithm** (see Figure 10) will be distributed to all clinicians to assist them with the assessment of patients with suspicious illnesses.

65. Diagnostic Algorithms will be distributed from the RSDRG via local Primary Care Trusts (PCTs) who will be responsible for adding contact details of local SDEs.

66. Clinicians should assess these patients according to the Diagnostic Algorithm – see Figure 10. If they are unable to exclude the diagnosis of smallpox, they should contact their local SDE to request a further assessment.
67. Whilst waiting for the SDE, the referring clinician should remain at the scene, isolate the patient as best as possible, and encourage close contacts of the patient also to remain close by.

68. SDEs will visit the patient, at the site, to make a further assessment. They should use appropriate personal protective equipment including non-sterile gloves, disposable gowns, face and eye protection and shoe covers.

69. There are three possible outcomes:
   
i. **Smallpox can be excluded**. The patient can be handed back to the referring clinician for further management.
   
ii. Smallpox cannot be excluded. The patient is now a **suspected case** of smallpox. Responsibility for management transfers to the SDE. The SDE should contact the RSDRT to arrange laboratory investigation and further management. Appropriate treatment for other possible diagnoses should be initiated.
   
iii. The clinical features are strongly suggestive of smallpox and there is no other likely diagnosis. The patient is now a **probable case** of smallpox. Responsibility for management transfers to the SDE. The SDE should contact the RSDRT to arrange immediate transfer to isolation facilities, laboratory investigation and further management (see paragraphs 82 to 88. Note that patients should not be transferred out of an ICU.

70. When they are contacted by an SDE, the RSDRT must immediately notify:
   
   - **The Designated Category 3 Regional Laboratory** (see Appendix 2) that they may expect specimens for EM – see paragraphs 77 to 78. The Regional laboratory will in turn immediately notify a Reference laboratory.
   
   - **The RE or RDPH**, who will in turn notify:
     - Local **police forces** - that there is a suspected case, and that escort to and security at the scene may be required.
     - Local **ambulance services** - that a Category 3 infectious removal may be required – see Appendix 5.
     - **Hospital isolation facilities** - that a bed may be required - see paragraphs 82 to 84.
     - The local Consultant in Communicable Disease Control (CCDC).
     - The local Health Emergency Planning Advisor.
     - The Communicable Diseases Surveillance Centre (CDSC) and the DH.
71. While awaiting the arrival of the RSDRT, and later while awaiting laboratory results, management of suspected or probable cases requires three key principals, irrespective of the site:

i. **Patient care.** The patient should be kept comfortable, and supportive treatment should be provided. This may necessitate transfer to isolation facilities at any stage – see paragraphs 82 to 84.

ii. **Infection control.** Entry and exit of persons and fomites from the potentially contaminated area must be strictly controlled. This may require the assistance of the police to maintain a protective cordon. Potentially contaminated fomites should be placed in yellow clinical waste bags at the earliest opportunity.

iii. **Preliminary identification of contacts.** The interval should be used for:
   - Establishing the date from which the patient should be regarded as potentially infectious – this is 24 hours prior to the time when the fever was first recognised (see paragraph 28).
   - Obtaining a detailed account of the patient’s movements while potentially infectious and during the incubation period. This is both in order to identify primary contacts, and to investigate potential sources of infection. (It is more difficult to get this information from the patient after admission to hospital).
   - Using this information to begin drawing up a list of primary contacts.
   - Contacts who are present at the site should be encouraged to stay there until smallpox can be excluded or confirmed. This is to facilitate infection control, and because they may then be given immediate vaccination by the RSDRT if smallpox is confirmed.

72. On contacting the RSDRT, the SDE may request that they visit the patient at the site to arrange laboratory investigation and further management, or that they arrange immediate transfer to isolation facilities (see paragraphs 81 to 84). The referring clinician should ideally stay at the site to assist clinical and public health management and because they will require vaccination if the case is confirmed.

73. **Immediate transfer** may be requested for probable cases of smallpox (unless already in ICU), or for suspected cases that are outside hospital but whose condition is causing concern or deteriorating.

74. The RSDRT will attend the patient, travelling in their own private vehicles, with their allocated equipment and supplies. The RSDRT paediatrician will only be required if the patient is under 16 years old.
75. The SDE may have elected to arrange transfer of the patient to isolation facilities before the RSDRT can arrive at the site. In this event:
   • The SDE should accompany the patient but must ensure that the referring clinician is able to maintain infection control measures at the site.
   • The RSDRT will split:
     □ The Medical Consultant and clinical nurse (and Paediatrician if appropriate) will join the patient at hospital isolation facilities.
     □ The Public Health Consultant and Communicable Disease Control Nurse will go to the site to ensure that infection control measures are maintained and begin contact identification and tracing.

76. When they reach the patient and/or site, responsibility for management transfers to the RSDRT, and at least one member of the Team should stay with the patient and at the site until smallpox can be confirmed or excluded.

77. After an assessment, the RSDRT will send diagnostic clinical specimens for EM (see Appendix 1). A minimum of four specimens of vesicle fluid should be sent to the nearest Designated Category 3 Regional laboratory, or directly to a Reference laboratory if this is closer.

78. One member of the RSDRT will personally transport specimens. On receipt of the specimens the Regional laboratory will immediately dispatch at least two of them to a Reference laboratory for confirmatory tests. Transport of specimens from the field to Regional laboratories and from Regional to Reference laboratories may require a blue light escort for speed.

79. If diagnoses other than smallpox are also considered possible, the RSDRT will send additional relevant specimens and initiate or continue appropriate treatments according to normal procedures.

80. Further specific management depends on the location of the patient, and is described in Figures 1 to 7. The on duty RSDRT will attend and commence clinical and public health management of suspected or probable cases. If they are required to spend long periods at the site whilst awaiting results, if their workload becomes excessive, or if additional suspected or probable cases arise, they may call for support from other RSDRTs in the same or adjacent regions.

81. EM results will be available within 6 hours of dispatch of specimens from anywhere in the UK. There are three potential EM results:
i. Organism other than smallpox detected (eg. VZV or HSV) – this may be regarded as a **negative result**. The SDE and RSDRT should refer the patient to appropriate local services.

ii. No organism detected – this should be regarded as an **equivocal result**, and the diagnosis of smallpox should not be excluded until there has been confirmation by a Reference laboratory.

iii. Orthopox particles detected – this should be regarded as a provisionally positive result, indicating a **probable case**, pending a confirmation by the Reference laboratory.

### Further action in the event of initial probable cases

82. The patient will be transferred to isolation facilities if this has not already happened. Ideally, one of the **High Security Infectious Disease Units** (Coppett’s Wood or Newcastle) should be used. However, it may be necessary to use an alternative ID unit if:
   - The patient’s life will be put at risk by a prolonged ambulance transfer.
   - There are large numbers of initial probable or confirmed cases and the high security units are full.

83. RSRDGs should therefore **examine local hospital isolation facilities** to determine which ones might be used for the care of initial probable cases of smallpox. Facilities should meet the minimum specifications outlined in Appendix 5.

84. The patient will be transferred in an ambulance, using standard procedures for a **Category 3 infectious removal**, accompanied by the RSDRT Medical Consultant, Clinical Nurse, and Paediatrician if appropriate (see also Appendix 6). A police escort is likely to be required. One relative or friend (a parent if the case is a child) may also accompany the patient.

85. After the ambulance crew have delivered the patient to the isolation facilities, they will park in a secure area, wipe the vehicle with disinfectant (0.1% hypochlorite) and then lock it. They will then remove and dispose of protective clothing, and shower and change where these facilities are available. They will then leave their contact details with RSDRT before going off shift pending PCR results. If PCR is positive they will be vaccinated immediately. The vehicle will require decontamination – see Appendix 15. It should not be reused until smallpox has been excluded or decontamination has been completed.
86. The RSDRT Public Health Physician and/or Communicable Disease Control Nurse will remain at the site to ensure that infection control measures are maintained, continue contact identification and tracing, and begin vaccinating contacts if the case is confirmed.

87. Diagnosis of a probable case will lead to mobilisation of a public health response including preparation of Smallpox Care Centres and Smallpox Vaccination Centres, contact tracing (see Section VII) and deployment and distribution of vaccine supplies (see Appendix 11). However, vaccination should be deferred until confirmation by PCR.

88. PCR results will be available within 12 hours of dispatch of specimens from anywhere in the UK. A positive PCR is required for confirmation of initial cases. However, in a case with strongly suggestive clinical features and no other diagnosis, smallpox should not automatically be excluded on the basis of a negative PCR result. The case should be reviewed and laboratory tests repeated if necessary.

Further action in the event of initial confirmed cases

89. Until further staff can be immunised, care of the initial confirmed cases, first at hospital isolation facilities and then at Smallpox Care Centres will have to be carried out by RSDRT members supported by SDEs.

90. The site will need to be evacuated and sealed until it can be decontaminated (see Appendix 15).

91. National and Regional Smallpox Outbreak Co-ordination Centres (NSOCC and RSOCC) will be convened to co-ordinate the public health response and monitor the epidemiological picture. NSOCC will alert international authorities.

92. Major control plans will be initiated with a response at local, regional and national level as described in Deliberate Release of Biological and Chemical Agents (DH; March 2000).

93. Rapid health alerts will be sent out for enhanced surveillance for other cases – see Section IX. This will include activation of NHS direct advice algorithms.

94. Designated Smallpox Care Centres (see Appendix 6) will be activated at the earliest opportunity, as these will be required to receive new patients once the high security beds are occupied. They will be need to be opened within 24 hours of confirmation of the first case.
95. Designated Smallpox Vaccination Centres will also be activated as soon as possible. These will be required for vaccination of contacts of cases.

96. Vaccination of contacts will proceed. Further healthcare, laboratory, emergency and other essential staff, including a large number of additional RSDRTs and SDEs, will be vaccinated to allow a response to multiple cases arising simultaneously.

**Cases arising in hospital**

97. Cases may be detected in A+Es, general hospital wards, ICUs or ID units. The procedures for managing such cases is summarised in Figures 3 to 6. Contacts in the hospital may be particularly susceptible to infection due to immunosuppressive disorders or treatments, or general ill health. Attack rates in hospital outbreaks of smallpox have been high.

98. If a patient with a suspicious illness is recognised, the Hospital Infection Control Team and Trust Management should be informed as early as possible. Hospital air conditioning systems should be turned off immediately and remain off until smallpox has been excluded or decontamination completed. This may necessitate deployment of alternative cooling facilities.

99. The Hospital Infection Control Team should assist the RSDRT in identifying all areas that the patient has passed through in order to guide implementation of infection control measures. The RSDRT has executive authority, through the RDPH, to implement whatever infection control measures are deemed necessary, including closure of the hospital.

100. Identification of contacts will require consideration of airflows within the hospital. Tracing of contacts will include other inpatients, discharged patients who were in contact with the case during their hospital stay, visitors to the hospital, and staff. Vaccination should be prioritised to those who have had the closest and most prolonged contact with cases.

101. Inpatient close contacts will require cohort observation, with strict infection control procedures observed to avoid spreading infection from any secondary cases that develop. Special consideration for the management of sick inpatient contacts will be required, bearing in mind contraindications to vaccination. Note also that early symptoms of smallpox may be masked by other underlying medical disorders.
102. It may be necessary to close large areas of the hospital to admissions, and restrict access to essential staff only, until all inpatient contacts are free of disease for 16 days after their last exposure to infection, since secondary cases may arise elsewhere in the building during the incubation period.

103. Depending on the structure of the hospital, and airflow within it, consideration may be given to vaccinating all patients, visitors, staff and others who have been present in the building with a infectious case.

104. At Alert Level 0, Hospital Infection Control Teams should examine their hospitals’ plans to determine airflows so that they are prepared for contagious pathogens. In the event of a case of smallpox, this will enable risk areas to be determined rapidly, allowing vaccination to be prioritised and disruption to be kept to a minimum.

105. Decontamination may necessitate prolonged closure of large areas of the hospital. Alternative facilities for healthcare provisions will be required.

**Cases arising at Port Health Control Units**

106. It is unlikely that a case will present at an airport since by the time the clinical features of smallpox are apparent, the patient is likely to be too ill to travel. It is possible that a case could present at a seaport. The procedures for managing such cases is summarised in Figure 7.

107. In the event of a case presenting at a port it would be possible to hold both the case and contacts against their will, as the Port Medical Officer (PMO) can advise the immigration authorities that passengers should not be allowed to enter the country.

108. Figure 7 assumes that the Infectious Disease (Aircraft) Regulations or the Infectious Disease (Ships) Regulations have not resulted in prior notification of the case to the Port Health Authorities and the case has presented at the health control unit. *If there is prior notification* to Port Health Authorities, then the PMO should board the aircraft or ship, and no one should be allowed to leave until an assessment has been made and the diagnosis confirmed or excluded. If the diagnosis is confirmed then all those on the same plane should be treated as category A contacts. Contacts on a ship may be category A or B depending on proximity and duration of exposure.
VII Management of cases and contacts during an outbreak

Co-ordination of the public health response

109. Isolation of cases and effective identification, tracing, vaccination and monitoring of contacts is essential to prevent the spread of infection. Any delay in intervention is likely to make a large impact on the size of the outbreak. Procedures for management of cases and contacts are summarised in Figure 8.

110. In order that these activities are properly organised, National and Regional Smallpox Outbreak Co-ordination Centres (NSOCC and RSOCCs) will be established following the first confirmed case of smallpox. RSOCCs will be required in all Regions since cases in one Region may have contacts anywhere in the country.

111. NSOCC will be located in the emergency room of CDSC until April 1 2003, and from then on in the emergency room of the HPA. It will be accountable to the DH.

112. NSOCC will include representatives from the following agencies and groups:
   - CDSC –
   - CPHL –
   - DH; EPCU –
   - DH; PH6 –
   - HPA (when established) –
   - CAMR -
   - Press office –
   - ID physicians and other clinical advisors –
   - Scientific and technical staff, administrative and support staff will be drawn from CDSC and the DH.

113. The role of NSOCC is the collation and analysis of epidemiological and laboratory information to assist identification of contacts and the source of infection, and the overall co-ordination of the public health response.

114. RSOCCs will evolve from RSDRGs and will be headed by Regional Epidemiologists (REs) on behalf of RDPHs. RSOCCs will fall within the Joint Health Advisory Cell. RSOCCs will be accountable to NSOCC.
115. RSOCCs will include members of the RSDRGs and in addition representatives from the agencies and groups listed below.
   • Regional HPAs
   • Regional Standard Government Offices
   • PCTs and Acute Trusts - including Communicable Disease Control consultants and nurses, ID physicians, frontline clinicians, virologists, hospital infection control specialists and others as appropriate.
   • Data handling, administrative and support staff will be drawn from Regional HPAs and Standard Government Offices.

116. The role of RSOCCs is to:
   • Co-ordinate assessment and management of cases – through the Regional network of SDEs.
   • Identify and trace contacts, and arrange vaccination and monitoring of contacts.
   • Monitor side effects of vaccination.
   • Establish essential communication lines (see Section X)
   • Arrange vaccination of essential personnel.
   • Ensure infection control including decontamination of affected areas.
   • Collect information about the movement of smallpox cases during the incubation period to help identify the source of infection.

117. Lines of communication and accountability between NSOCC, RSOCCs and local clinical, laboratory and public health services are summarised in Figure 9.

**Isolation of cases**

118. Cases may arise in individuals who are being monitored as contacts, or in individuals who have no known epidemiological link to other cases.

119. **Probable and confirmed cases** will be transferred directly to a treatment ward at a Smallpox Care Centre as soon as this is available.

120. **Possible cases** will be transferred to an observation ward at a Smallpox Care Centre until the diagnosis of smallpox can be confirmed or excluded. Some of these may be due to side effects of smallpox vaccine.

121. A large number of **suspicious illnesses** are likely to be reported to RSOCC due to heightened awareness and anxiety among clinicians. These should be assessed and managed as during Alert Levels 0 and 1 with assessment by a SDE and further management by an RSDRT if necessary.
Care of cases

122. Smallpox is a severe viral infection, the care of which has three main components:
• Clinical care and support for the sick patients.
• Maintenance of infection control during the infectious period – see Appendix 7.
• Providing adequate healthcare input to ensure continued care until the patient is convalescent.

123. No antiviral drug is currently known to be effective against smallpox virus. It must therefore be assumed that patients suffering from smallpox will require support through the natural course of infection. Cidofuvir has been used to successfully treat the orthopox infections *molluscum contagiosum* and *orf* in humans. The effectiveness of the drug against established smallpox disease is unknown. Depending on supplies, it may be available as a therapeutic option in some cases.

124. In the presence of multiple organ failure, there is unfortunately no additional benefit from treatment in ICU, and transfer to ICU should be avoided in order to contain the infection.

125. Those who are unimmunised will suffer disease of varying severity, of which about 40% will be severe or ‘fulminant’, with an overall case-fatality rate of 25-40%.

126. Vaccinated individuals who become ill despite vaccination suffer mild or moderate disease in 95% of cases, with a case-fatality rate of less than 1%.

127. Those with severe disease will require pain relief, hydration, nutrition and airways support during the early part of the illness, maintenance of personal hygiene and skin care during the rash phase, and treatment for secondary bacterial infections if necessary. Patients with milder disease may remain self-caring in many respects, but should be isolated while infectious, to reduce the risk of generating further cases.

128. The early rash is accompanied by red and blistering lesions in the throat and upper airway. In severe cases, these can be extremely painful, leading to excessive salivation, throat swelling and difficulty in swallowing. Opiate analgesics may be required. If throat swelling threatens the airway, boluses of hydrocortisone may be given to relieve oedema, as for croup or bronchiolitis. The dose for an adult is 200mg intravenously, for a child, 5 mg/kg is often adequate. Although corticosteroids may reduce fever, they have little effect on the evolution of the illness, and do not worsen the outcome of established viral diseases.
129. Oral hydration, and nutrition with soft food, is preferable as long as it can be adequately maintained. Intravenous hydration is possible in many cases, but a severe skin rash makes the care and maintenance of a peripheral intravenous cannula difficult. It may then be necessary to install a central venous cannula, which will require appropriately trained and vaccinated staff and radiological confirmation of correct positioning of the line.

130. An extensive rash will result in widespread exudation and crusting, including the scalp area. It may be beneficial to cut the hair short before this happens, to facilitate the shedding of crust and scabs, and to facilitate the maintenance of skin hygiene. Skin swelling can be a major problem, due to the extensive, deep-seated lesions. It is strongly advisable to remove rings and other body jewellery at the onset of the rash, to avoid constriction and ischaemia of digits or of other body areas. The more severe and extensive rashes are painful, and analgesia should be provided.

131. Skin hygiene contributes importantly to the avoidance of secondary infection, but infection of broken vesicles and pustules, and of denuded skin areas with *Staphylococcus aureus* or *Streptococcus pyogenes* cannot be avoided in all cases.

132. Treatment with oral or parenteral flucloxacillin or co-amoxyclov is appropriate (oral clindamycin is an alternative, with a higher risk of diarrhoeal adverse effects; co-trimoxazole is a second choice, with a risk of skin, bone-marrow or liver toxicity, particularly in older adults).

133. Hospital-acquired resistant organisms such as MRSA may require treatment based on the result of culture and sensitivity data. Further antibiotics may be appropriate according to the patient’s clinical condition: cefuroxime axetil or cephadrine orally for mild skin infections, injected cefuroxime for more severe infections of skin, chest and urinary tract (alternative to co-amoxyclov). Daily IM or IV teicoplanin is often very effective in both sensitive and resistant Gram-positive infections (including MRSA) and not too labour-intensive to administer.

134. Secondary bacterial infection of the respiratory tract is much less common, but may be caused by staphylococci or streptococci or rarely *Haemophilus influenzae*. Co-amoxyclov, cefuroxime or levofloxacin (or co-trimoxazole as second choice as above) are appropriate oral antibiotics in this situation.

135. There is often mild conjunctivitis, which requires no specific treatment. Pocks may affect the conjunctiva, but usually heal without affecting sight. The eyes may be closed by oedema as the rash reaches its height. Eye toilet using sterile saline is then helpful. Chloramphenicol eye ointment may be given for short periods of time if secondary bacterial conjunctivitis occurs.
136. As the fever subsides and the rash begins to heal, the patient will gradually become more mobile. Emotional support may be required at this stage, especially if there is significant facial scarring.

137. The need for continued isolation, until scabs have all been shed, may also be very trying for patients who are mobilising well. The last deep scabs (or 'seeds') tend to remain in the thick skin of the soles of the feet. In some circumstances it may be beneficial to remove these, using a needle to release them from hardened pockets of skin. The patient who is free of scabs can be released from isolation.

**Smallpox care centres**

138. Buildings suitable for use as smallpox care centres will be identified in each Region, at Alert Level 0, by the RSDRG.

139. Minimum specifications for these facilities and procedures for transport of patients are summarised in Appendix 6.

140. RSDPGs will identify, at Alert Level 0, doctors, nurses and support staff who would be willing to work in smallpox care centres. Ideally they should have been previously vaccinated so that they could be revaccinated with a faster immune response and a lower incidence of side effects.

141. Observation and treatment wards will be maintained separately to ensure that possible cases are not exposed to infection.

142. All possible and probable cases will be vaccinated on admission to protect them from infection by confirmed cases if the diagnosis of smallpox is subsequently excluded.

**Contacts: classification and management**

143. Rapid identification and tracing of contacts is essential since vaccination should be carried out as soon as possible, and at most within 3 days of exposure to infection, because the degree of protection diminishes as the interval between exposure and vaccination increases. Contacts should be checked for symptoms before vaccination, to ensure that they are not co-primary cases.
144. If the diagnosis of smallpox in possible or probable cases is subsequently excluded, contacts who have been identified but not yet traced need not be vaccinated or followed up further.

145. **Primary contacts** are persons who have had contact with confirmed cases of smallpox during the infectious period or contaminated fomites. As a precaution, the infectious period should be regarded as from 24 hours prior to the first recognised symptoms until the last scab has been shed.

146. Primary contacts may be divided into two categories, A and B according to their risk of infection. These categories should be regarded as a guide: **individuals’ risk of infection should always be considered in the context of the proximity and duration of exposure.**

147. Contacts may be **asymptomatic** or **symptomatic**. Symptomatic contacts are people who fit the contact definitions, and in addition have prodromal symptoms that may indicate early smallpox infection. These are prolonged high fever (above 38°C) and/or constitutional symptoms such as prostration, severe headache or backache, rigors and generalised maculopapular rash.

148. **Secondary contacts** are people in close contact with category A primary contacts.

**Category A primary contacts (highest risk of infection)**

**Definition**

149. These are people who are likely to have been exposed to infection through large droplets or contaminated fomites. They include:

- **Household contacts**: all persons usually resident at the same address as infectious cases of smallpox, and other visitors who have spent substantial periods of time at this address during the infectious period. Note that in documented outbreaks the secondary attack rate among household contacts was around 50%.

- **Face to face contacts**: all persons who have had prolonged interactions with infectious cases of smallpox within a distance of 2 metres (6.5 feet). These may include contacts at work, in social settings, and unvaccinated healthcare and emergency workers.

- **Fomite contacts**: all persons who have had direct contact with clothing or articles that have recently been used by infectious cases of smallpox. Again these may include contacts at work, in social settings, and unvaccinated healthcare and emergency workers.
As a prompt, category A contacts may be identified by asking about family members, relatives, close friends and close work colleagues who may have had contact with infectious cases of smallpox.

Other persons thought to have shared a common exposure with cases of smallpox, including the initial release of the virus.

Management and monitoring

150. Category A contacts should be vaccinated as a matter of urgency.

151. Category A contacts must be formally monitored for the development of symptoms for a period of 16 days from the last exposure to an infectious case.

152. Formal monitoring involves daily recording of body temperature, measured orally, and daily reporting of this, and the presence of other constitutional symptoms to a designated Smallpox Contacts Telephone Number, which will be dedicated solely for this purpose. Arrangements for establishing this are described in Section X.

153. An oral thermometer (preferably a plastic model that can be disposed of after the formal monitoring period), a temperature chart, instructions on the measurement and recording of body temperature, general advice, and the Smallpox Contacts Telephone Number will be provided (see Appendix 17). In addition, a mobile telephone will be provided to those who do not have access to a mobile or land telephone at home.

154. Category A contacts who fail to make their daily health report will be actively traced, by telephone or in person.

Restrictions on activity

155. Category A contacts who develop a fever or other constitutional symptoms must stay at home and immediately telephone the Smallpox Contacts Telephone Number.

156. The Restriction Period is the time during which category A contacts are at greatest risk of developing symptoms and becoming infectious. The incubation period for smallpox is usually 10 to 16 days, and as a precaution patients should be regarded as infectious from 24 hours prior to the first recognition of symptoms.
157. The Restriction Period therefore extends from 9 days after the first exposure until 16 days after the last exposure to an infectious case. During this time, restrictions on activity of category A contacts apply, they must:
- Stay away from work or school.
- Avoid contact with unvaccinated individuals.
- Remain within their local area.

158. Outside the restriction period, and as long as they are well, category A contacts may continue normal activities, although they must not travel abroad and should be advised to stay within their local area until the end of the formal monitoring period and until their vaccination site has completely healed.

159. There is no legislation to enforce compliance with restrictions on activity. However, in what will be a mainly susceptible population, the onset of symptoms in smallpox cases will be rapid and debilitating, and the patient is unlikely to continue their normal activities.

**Action to be taken in the event of symptoms**

160. Category A contacts who develop prodromal symptoms (see paragraph 147) should be regarded as possible cases and transferred immediately to the observation ward of a smallpox care centre. Those who also develop a vesicular rash should be regarded as probable cases and transferred to the treatment ward.

### Category B primary contacts (lower risk of infection)

**Definition**

161. These are people who have a lower chance of having been exposed to infection via aerosol. They include all persons who have shared rooms or other enclosed spaces with infectious cases of smallpox, and who do not fall into the groups of face to face or fomite contacts described in paragraph 149.

162. These may include work colleagues, and people who have visited the same premises or travelled on the same public transport (buses, trains, tubes and planes) as smallpox cases. People who have shared air-conditioned buildings with infectious cases should be managed as category B contacts. Note however that transient or distant contacts (see paragraphs 173 to 177 should not be managed as category B contacts. NSOCC will provide further advice as required to assist identification of category B contacts.
Management and monitoring

163. Category B contacts should be vaccinated unless they have contraindications in which case the risk from vaccination should be weighed against the risk from disease (see paragraph 186).

164. Category B contacts do not require formal monitoring. However, their details should be recorded, and they should be given an advice sheet (see Appendix 17) including the Smallpox Contacts Telephone Number (see Section X) that they must call immediately if they develop a fever or other constitutional symptoms during the 16 days following their last exposure to infection.

Restrictions on activity

165. Category B contacts who have a fever or other constitutional symptoms must stay at home and call the smallpox contacts telephone number. Otherwise no restrictions on activity are necessary although they must not travel abroad until they have been free of symptoms for 16 days following their last exposure to infection, and until their vaccination site has completely healed.

Action to be taken in the event of symptoms

166. Category B contacts who develop prodromal symptoms (see paragraph 147) should be regarded as possible cases and transferred immediately to the observation ward of the smallpox care centre. Those who also develop a vesicular rash should be regarded as probable cases and transferred to the treatment ward.

Secondary contacts

Definition

167. These are people who will have ongoing household contact with category A primary contacts during the formal monitoring period.

168. They may therefore be exposed to infection if the primary contact becomes symptomatic. They include all persons usually resident at the same address as the primary contact, and other visitors who will be required to spend substantial periods of time at this address during the formal monitoring period.
Management

169. All secondary contacts of category A contacts should be vaccinated.

170. If they have any contraindications to vaccination (see Appendix 9) then they should avoid contact with the primary contact until the primary contact’s vaccination site is completely healed because of the risk of transfer of vaccinia infection. This may mean leaving the house.

171. No monitoring or restrictions on activity are necessary unless the primary contact becomes symptomatic, and therefore becomes a possible or probable case.

172. If smallpox is confirmed in the primary contact, then the secondary contacts become category A contacts themselves and must be managed accordingly.

Transient and distant contacts (no risk of infection)

173. There may be large numbers of people who are concerned about having been exposed though brief or remote contact with smallpox cases but who do not fall into the groups of face to face or fomite contacts described in paragraph 149 or the group of category B contacts described in paragraph 162, and are therefore not at risk of infection.

174. These may include passing contacts for example in the street or shops, and people who have spent short periods of time in large well ventilated areas with smallpox cases.

175. These individuals do not need to be traced and do not require vaccination. However, they may identify themselves once details of the case become public. Their details should then be recorded, and they should be given an advice sheet for reassurance (see Appendix 17).

176. These individuals should not be offered vaccination because this would divert resources away from the essential measures of tracing and vaccinating all category A and B contacts.

177. If they develop fever or other constitutional symptoms they may call a Smallpox Advice Line (not the Smallpox Contacts Telephone Number), which will be set up for providing advice to the general public.
Identification and tracing of contacts

178. SDEs, RSDRTs and clinicians at Smallpox Care Centres will establish the time from which cases of smallpox have been infectious. They will then:
   • Compile a list of household contacts.
   • Obtain a detailed account of the patient’s movements during the infectious and incubation periods. This is both in order to identify other primary contacts, and to investigate potential sources of infection.

179. Information about household contacts and the patient’s movements during the infectious period will be passed to the RSDRG or RSOCC for further investigation and action.

180. Vaccination and monitoring of household contacts can be arranged immediately. Other category A and B contacts will need to be traced urgently so that vaccination and monitoring can be arranged. This will be done through CsCDC. TB nurses and Health Advisors have considerable experience at this, which may be usefully employed.

181. It may be possible to trace contacts through official lists and social networks. However, if this is not possible, consideration should be given to a making a public announcement asking contacts to identify themselves. This should be done with consideration to maintaining the confidentiality of smallpox patients.

182. A Smallpox Contact Tracing Number (see Section X) will be required so that contacts can identify themselves to RSOCC. They may also identify themselves to their GP or through NHS Direct, which will help to categorise contacts by using telephone triage to grade individuals’ risk of exposure to infection.

183. Once arrangements for formal monitoring of category A contacts have been made, secondary contacts can be identified.

184. Full details of all contacts identified will be recorded on a database along with the management and outcome of each.

Vaccination of contacts

185. Contacts should be assessed for contraindications prior to vaccination. They should also be examined for active skin conditions and other medical disorders that may be confused with smallpox, so that the occurrence of new symptoms can be distinguished.
186. There are no absolute contraindications to vaccination. Contacts with relative contraindications should be assessed to determine whether the risk from disease outweighs the risk from adverse effects of vaccination. This will be done at Smallpox Vaccination Centres by vaccinators with access to expert immunological advice. If vaccination is indicated, depending on supplies, they may be given Vaccinia Immunoglobulin (VaIG – see Appendix 13) to prevent vaccine complications. Adverse effects may be treated with cidofuvir - see Appendix 14.

Arrangements for vaccination

187. Vaccination will be carried out at Smallpox Vaccination Centres - see Appendix 8. Suitable sites will be identified by RSDRGs at Alert Level 0 so that Centres can be activated immediately if required.

188. Arrangements for the distribution (see Appendix 11) and administration (see Appendix 12) of vaccine must ensure the security of vaccine supplies and staff. Information, consent forms and certificates for vaccinees are in Appendix 16.

189. Vaccination of different groups (healthcare, emergency and essential workers, and contacts) will be required, and a strict triage system will be necessary to ensure prioritisation of vaccine supplies.

190. All those vaccinated will be assessed on the third day following vaccination to determine whether a papule has formed (see Appendix 12).

191. Category A contacts will be asked to return to the Smallpox Vaccination Centre for assessment of their papule by a trained clinician. Category B and secondary contacts will be given written instructions describing what the papule should look like. They need only return to the Smallpox Vaccination Centre for professional assessment if they are concerned that their papule has not formed.

192. Vaccinated individuals shed vaccinia virus until the pock has completely healed. Individuals who have been vaccinated should avoid contact with others who may be at risk from vaccinia. These are: people who are immunosuppressed, people with eczema and pregnant women. Individuals with these disorders who normally live in the same household as vaccinees should move to alternative accommodation.
Unimmunised primary contacts

193. These include primary contacts who refuse vaccine, fail to respond to vaccination, or who are vaccinated late (more than 3 days after their first exposure to infection).

194. Primary contacts who fail to show a response to a first dose of vaccine after 3 days should be revaccinated and the dose discounted.

195. Non-responders and those vaccinated late may be given additional prophylaxis against smallpox concurrently with (re) vaccination in an effort to attenuate disease. Supplies of additional prophylactic treatments should be prioritised to those most at risk of disease:
   - Contacts vaccinated between 3 and 8 days after first exposure to infection may be given VaIG (see Appendix 13).
   - Contacts vaccinated more than 8 days after first exposure may be given cidofuvir (see Appendix 14).

196. Unimmunised primary contacts will also require additional monitoring and/or restrictions on movement:
   - Those in category A will be asked to stay in isolation accommodation until the end of the incubation period.
   - Those in category B should be followed up as category A contacts with a period of formal monitoring and identification and vaccination of secondary contacts.

197. Isolation accommodation will be required for unimmunised category A contacts. Appropriate facilities will need to be identified, and may include local hotels, university halls of residence etc.

Special issues relating to contacts

198. Individuals in certain groups such as illegal immigrants and overstayers, and homeless persons may pose problems. If they are cases, they may be reluctant to trust and engage with healthcare services when they become ill, thereby delaying access to healthcare and exposing more contacts. If they are contacts, their details may not be passed on by smallpox cases, even if they are close contacts, which may mean that vaccination is delayed or overlooked. There could be difficulties explaining the need for admission to a centre, restricting their movements and logistical issues of monitoring for the development of fever.
199. Clear advice is therefore needed to emphasise the severity of the problem, and guarantees may be required to protect the confidentiality of contacts, and possibly to protect illegal immigrants and overstayers from prosecution. Engagement through voluntary and community groups may be effective. Interpreters should be available locally, and information sheets for those for whom English is a second language have been drawn up.
VIII Vaccination

General Principles

200. Vaccine against smallpox contains a live virus, vaccinia, which produces cross immunity against variola major and minor.

201. Targeted vaccination and monitoring of contacts, together with isolation of cases, is the mainstay of containment. The efficacy of vaccination in preventing spread of the disease depends on early detection of cases and identification and tracing of contacts. This strategy of ring vaccination is compatible with WHO recommendations.

202. Smallpox vaccination carries a risk of complications, which occurred at a higher frequency than that now acceptable for a modern vaccine. These complications occurred more frequently in people who were immunosuppressed, people with eczema and pregnant women. Because of this, mass vaccination of the population is not a first line option either prior to or in the event of an outbreak.

203. There is a need to consider protection of close contacts of people who have been vaccinated in view of shedding of vaccinia virus (eg. children with eczema should not share a house with someone who has been vaccinated until their vaccination site has completely healed).

Efficacy and take rate

204. Successful vaccination produces a characteristic papule after 3 days. This evolves into a vesicle at 4 to 5 days and a pustule at 6 to 7 days. The pustule is a reliable indication that protective antibody levels have developed – ie. there has been a successful “take”. A more rapid response is seen in persons who have had previous vaccination.

205. Take rates depend, amongst other things, on potency of vaccine, age of vaccinee, past vaccination history and vaccination technique.

206. For primary vaccination, take rates have historically varied from 85% to 99.9%. The primary take rate of an appropriately potent (10^8 pock-forming unit/ml) and properly administered vaccine is likely to be greater than 99%.
207. For revaccination, take rates have been lower, from 54% to 93% with a mean of about 70%. With the cessation of routine vaccination so long ago now, residual immunity is likely to be negligible, and any vaccination now is likely to resemble the primary vaccinations of the past.

208. For pre-exposure vaccination, a successful “take” provides full protection against smallpox. Post-exposure vaccination given up to 3 days after exposure also provides protection, although it may not completely prevent infection, and patients may develop mild modified disease.

**Contraindications and complications**

209. Contraindications to vaccination include eczema, immunosuppression and pregnancy, among others. Full details can be found in Appendix 9.

210. Serious adverse effects associated with vaccination include inadvertent inoculation at other sites, generalized vaccinia, eczema vaccinatum, progressive vaccinia and post-vaccination encephalitis. Full details can be found in Appendix 10.

211. Surveys from the US have found that the overall risk of serious adverse events was between 50 and 1000 per million vaccinees, with inadvertent inoculation and generalised vaccinia the most common complications ([http://www.bt.cdc.gov/agent/smallpox/vaccine-safety/adverse-events-chart.asp](http://www.bt.cdc.gov/agent/smallpox/vaccine-safety/adverse-events-chart.asp)).

212. However, this data may not be directly applicable to the current UK situation:
   - A different strain of vaccine virus will be used (Lister instead of New York Board of Health)
   - There are more people at risk of adverse effects because the prevalence of eczema and immunosuppression is higher than in the survey populations.
   - The incidence of complications is up to ten times higher in primary vaccinees than re-vaccinees.

213. In the same surveys, the risk of fatal complications was approximately one per million in primary vaccinees. In a study in England and Wales in the 1950s it was estimated at three per million. Death is most often the result of postvaccinial encephalitis or progressive vaccinia. Fatal complications occur in approximately one per four million in re-vaccinees.
Vaccination strategies at progressive Alert levels

Vaccination strategy at Alert Level 0

214. The risk of adverse effects of vaccination must be balanced against the risk of leaving vulnerable those specialist healthcare and laboratory workers who would be first to be exposed in the event of a case and who would not have adequate time for vaccination to become fully effective. Some specialist healthcare and laboratory workers will therefore need to be vaccinated at Alert Level 0 to act as a first line of defence, even without an identifiable, specific threat. In the event of a case occurring, they will then be able to make the diagnosis, care for the patient, analyse clinical specimen, and initiate public health action to contain the outbreak.

215. Those vaccinated at Alert Level 0 will be:
- Two staff at each of the Designated Category 3 Regional laboratories where diagnostic clinical specimens may be sent for EM diagnosis – see Appendix 2. (Staff at the two Reference laboratories are already routinely vaccinated to protect them against other orthopox infections.)
- The RSDRTs: each will have 5 clinical roles and 5 people per role on a rota – see paragraph 58.
- The SDEs – see paragraph 60.
- Vaccinators – see paragraph 228.

Vaccination strategy at Alert Level 1

216. If the event of a heightened threat, a greater number of healthcare, emergency, laboratory and other essential personnel will be vaccinated, including all those who are likely to be directly involved in the assessment, management and investigation of smallpox cases:
- Additional RSDRTs and SDEs.
- Front-line clinical staff including designated ambulance workers.
- Medical, nursing and support staff (porters, cooks, cleaners, laundry etc) who might be required to work at Smallpox Care Centres.
- All laboratory staff who might be required to receive diagnostic clinical specimens (for EM and/or PCR).
- Epidemiological staff who might be involved in contact tracing.
- Mortuary staff who might be required to handle infected bodies.
- Environmental health officers who may be required to decontaminate premises.
- Individuals who might be required to join NSOCC or RSOCCs.
- Additional vaccinators.
217. RSDRGs should identify these personnel within their Region at Alert Level 0. If possible, individuals should have received smallpox vaccine in the past, as they will have a faster immune response and a lower incidence of side effects.

**Vaccination strategy at Alert Levels 2 and 3**

218. In the event of confirmed smallpox in the UK, healthcare, emergency, laboratory and other essential personnel will be vaccinated as at Alert Level 1. The household contacts of these personnel will also be vaccinated.

219. In addition, other key workers (such as police and fire service personnel) may be vaccinated. These will be defined as required by the DH, and then identified by RSOCCs who will be responsible for arranging vaccination.

220. Smallpox Vaccination Centres will be activated on confirmation of the first confirmed case for vaccination of contacts of cases. Vaccination will be provided by nurses trained as vaccinators.

221. Clinicians should resist offering vaccination to individuals who demand vaccination without an epidemiological indication – i.e. they do not fall into the groups of category A and B contacts.

222. Vaccination may be considered for travellers from the UK to infected countries, or from the UK in the event of an outbreak to countries that remain smallpox free. However this may be a major undertaking given the volume of travellers, and would be a low priority for use of vaccination resources.

**Vaccination strategy at Alert Level 4**

223. Circumstances may arise when mass vaccination may be required to raise the level of immunity to smallpox:
   - A large number of cases occurring simultaneously all over the country. (Uncontrolled spread resulting from large or multiple deliberate release.)
   - Many secondary cases occurring without identifiable contact with a primary case, implying that contact tracing and enhanced surveillance for cases has been ineffective.

224. Public demand may also influence the decision to implement mass vaccination. General public demand for vaccination is not necessarily inevitable if public relations are good from the outset – see Section X.
Decisions about whether to implement mass vaccination must be taken with due consideration of:

- The risk of adverse effects from vaccination, which may exceed the risk from disease.
- Vaccination complications, especially generalised vaccinia, may create difficulties in the diagnosis of smallpox.
- Vaccination resources, including vaccine supplies; there is a danger that mass vaccination could divert resources from essential outbreak control measures.

It is planned that sufficient stocks will be available to vaccinate the entire population of the UK should this be necessary. Mass vaccination will only be implemented at the direction of the DH.

**Vaccination strategy at Alert Level 5**

Following an outbreak, at Alert Level 5, identified healthcare, emergency, laboratory and other essential personnel should be revaccinated annually, and in addition if they are re-exposed if this is more than 6 months since their last vaccination. Provided there are no contra-indications, the household contacts of these individuals should be encouraged to accept revaccination every three years.

**Vaccination of essential personnel**

Vaccination of essential personnel will be carried out by NHS occupational health nurses who have been trained as vaccinators and have themselves been immunised.

Essential personnel will be screened to ensure that neither they nor their household contacts has any contraindications to smallpox vaccine.

A central register of vaccinees will be maintained, and they may be asked to participate in research programmes to evaluate the vaccine.

An immune response will be verified before essential personnel are allowed to become involved in smallpox diagnosis, patient care, analysis of specimens or public health action.

Essential personnel will be revaccinated every 3 years at Alert Level 0 in order to guarantee immunity.
IX Enhanced surveillance following an outbreak

Identification of the source of infection

233. There may have been an overt release of virus. All those deemed to have been exposed, according to an evaluation at the site and time of release, will then be managed as category A contacts.

234. It is more likely that the virus will be released covertly. Detection of the location of the event will depend on analysis of information given by patients about their movements during the incubation period. This information will be collated and analysed by NSOCC in order to identify potential sources of infection, which may be other cases or the initial release.

235. If a potential source of infection is identified from common exposure histories, then others who have shared the same exposure should be regarded as category A contacts and traced as a matter of urgency.

Case finding following a release

236. At Alert Level 1, clinicians will be informed of the nature of the heightened threat, reminded of the presenting clinical features and case definitions, and the procedure for reporting and assessment of patients with suspicious illnesses (see Section VI).

237. At Alert Levels 2 and 3, cases may arise in individuals who are being monitored as contacts, or in individuals who have no known epidemiological link to other cases. The latter will be assessed by one of the expanded number of SDEs.

238. More intensive surveillance will be necessary to ensure that all cases are recognised and control measures implemented as early as possible. Clinicians will again be reminded of the presenting clinical features and case definitions, and the procedure for reporting and assessment of patients with suspicious illnesses (see Section VI).

239. SDEs will be issued with Smallpox Reporting Forms (see Appendix 16) including a Smallpox Reporting Telephone Number for reporting of suspected cases to RSOCC. Arrangements for establishing this telephone number are discussed in Section X.
240. Active surveillance of hospitals may be required in order to reliably exclude additional cases. All hospital inpatients with suspicious illness, and recent unexplained deaths, should be reviewed retrospectively to exclude the diagnosis of smallpox.

241. NHS Direct may be able to use algorithms combining details about symptoms and exposures in order to assess the significance of symptoms in concerned individuals and provide reassurance or referral to local experts if necessary.

**Handling data**

242. Even a small outbreak may generate considerable quantities of epidemiological data. Forms and tools to assist with the collection, collation and analysis of information about cases and contacts can be found in Appendix 16. These include:

- Smallpox reporting form.
- Contact identification and monitoring form.

*Need to expand this Section based on work at CAMR.*
X Communication

243. A smallpox outbreak will necessitate extensive communication activities. These will be run from the DH, by a team according to strategies and procedures that are defined before an event. Thus communication activities should have been occurring before any cases of smallpox are suspected, as well as strategies and procedures being in place should any cases arise.

Clinical, laboratory and epidemiological information

244. At Alert Level 0, Diagnostic Algorithms (see Figure 10), will be distributed to all clinicians from RSDRGs via PCTs who will be responsible for adding the contact details of local SDEs.

245. In the event of an Alert Level 2, the suggested channels of communication for exchange of information between NSOCC, RSOCCs and local clinical, laboratory and public health services are summarised in Figure 9.

246. A series of telephone numbers with a large number of lines will be required, which will need to be secure and dependable and able to cope with large call volumes. These are:

- **Smallpox Reporting Telephone Number** for clinicians to report suspected cases to RSOCCs. Number will be required in each Standard Government Region.
- **Smallpox Contacts Telephone Number** for category A and B contacts to report the presence of fever or other constitutional symptoms. This would be best set up at local level, with contacts reporting to RSOCC.
- **Smallpox Contact Tracing Number** to allow potential contacts to identify themselves to RSOCC following an announcement about exposures. They may also choose to identify themselves to their own GP or through NHS Direct, which may be able to grade individual’s risk of exposure to infection using telephone triage.
- **Smallpox Advice Number** for providing information to the general public. There are likely to be large numbers of “worried well” who may have symptoms and require reassurance. This information could also be provided through a dedicated website.
Public and media

247. Pre-event disclosure of relevant information as part of a phased response to a credible threat is essential to establish public trust and co-operation in the event of smallpox cases arising.

248. Prior to any smallpox case, there needs to be communication between the DH, HPA and local providers about these interim guidelines and their interpretation for local planning purposes, including information for the public and media responses.

249. There also needs to be inter-agency working at all levels with health and emergency services working with National, Regional and Local emergency planning departments so that their roles in communicating to the public and media are known and understood should cases of smallpox occur.

250. Good communication during an event can reduce public anxiety and enhance the workings of emergency service responders and health care workers. The public should understand that a plan is being followed and given explanations for various actions being undertaken. Therefore, one of the primary communication objectives is to instil and maintain public confidence by providing the public with information that addresses their questions, fears and concerns. General information about smallpox, and updates on the status of any outbreak could be provided on a dedicated website.

251. The purpose of smallpox communication plans should be to help local, regional and national public health staff effectively educate the public, health care professionals, policy makers, partner organisations and the media about smallpox, smallpox immunisation, and important health strategies related to smallpox (eg. isolation and restrictions of movements) prior to an outbreak or confirmed cases of smallpox.

252. Alert Level 0 Communication Activities

- Increase public, health care provider, public health official, policy maker, media and key partner knowledge and understanding of smallpox disease, smallpox immunisation, and the general approaches/concepts that will be used should there be a confirmed case or outbreak of smallpox; this includes isolation, immunisation strategies, and vaccine administration. Ideally, communications and education will help “de-mystify” smallpox and increase knowledge and understanding of isolating and restricting movements of smallpox patients.
- Start to build up relationships with key media personnel who can be used to convey information to the public in a rational way should an event occur.
Increase the range and type of smallpox materials available to the public, health care providers, policy makers, and the media.

Help prepare and establish appropriate public, health care provider, policy maker, and media responses to a smallpox case or outbreak, including an understanding of how the public health system will respond, roles and responsibilities of the different sectors involved, and reasonable expectations regarding the scope and effects of public health actions.

Establish the protocols that would be used to communicate the specific data that would need to be reported daily after a confirmed smallpox case (e.g., morbidity and mortality figures; geographic location of cases; number of contacts under surveillance etc.).

253. **Alert Level 1 Communication Activities**

- Explain the nature of the heightened threat and the response required.
- Continue and strengthen Alert Level 0 communication activities.

254. **Alert Level 2, 3 and 4 Communication Activities**

- Establish a **Central Communication Command Centre** at the DH:
  - A staffing assessment will be made and the Centre will be staffed by press officers from the DH and HPA for extended hours and days.
  - The Centre will work closely with NSOCC, which will provide information/materials that will enable it to respond to media, public, and health care provider inquiries. Twice-a-day briefings with these partners should be implemented.
  - The Centre will co-ordinate responses with Regional health press offices to ensure consistency of the information being given to the media.
  - The Centre should emphasise that the role of all agencies involved in the response to the outbreak is "to identify the public health threat and take actions to protect the public."

- Activate a dedicated smallpox website and make arrangements to update it regularly as events change.

- Arrange regular television bulletins by a “news-reader type” (preferably already known to the public) who has had training about smallpox. He or she will provide information regarding the situation, the major actions being taken, information about smallpox, public guidance, and resources etc.

- Rumour control will be a major main concern. Thus it will be imperative to immediately issue information updates and to correct, as much as possible, errors and misperceptions.

- Regional Directors of Public Health will be asked to designate press officers to co-ordinate communication and media activities and to work with the Central Communication Command Centre. **Unified, consistent public health**
messages will need to be given to the media, public and health care providers in the event of a smallpox outbreak.

Annex: key contacts

Reference Laboratories

**CPHL**

Dr David Brown  
Central Public Health Laboratory  
61 Colindale Avenue  
London  
NW9 5HT  
Tel: 020 8200 4400 ext 3018

**CAMR**

Special Pathogens Reference Unit  
Centre for Applied Microbiology & Research (CAMR)  
Porton Down  
Salisbury  
Wiltshire  
SP4 0JG  
Tel: 01980 612100 (out of hours ask for Diagnosis on call)

Approved courier for Hazard Group 4 organisms

Gosafe International Ltd  
Unit 15  
Shield Road  
Ashford  
Middlesex  
TW15 1AU  
Tel: 0879 600 0129